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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/724,620	11/28/00	TAYLOR R	9426-048

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EXAMINER	
CANELLA, K	
ART UNIT	**PAPER NUMBER**
1642	5

DATE MAILED: 11/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/724,620	Taylor et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-46* is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *23-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

1. Claims 1-22 have been canceled. Claims 23-46 have been added and are examined on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 23-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating or preventing cancer in an animal comprising administering an effective amount of anti-C3b(I) antibody, does not reasonably provide enablement for a method of treating or preventing cancer in an animal comprising administering an effective amount of multi-anti-C3b(I) antibodies, or an anti-C3b(I) antibodies which are immunospecific for C3b(I) linked to IgM or IgG bound to cancer cells, or anti-C3b(I) antibodies which are immunospecific for C3b(I) linked to proteins or lipids on cancer cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims. The specification teaches that C3b(I) is deposited on tumors. The specification teaches the anti-C3b(I) monoclonal antibodies of 7C12, 2H11, 8E11, which are of the IgG1 isotype, and the anti-C3b(I) monoclonal antibody of 3E7, also of the IgG1 isotype, which binds to an epitope of C3b(I) distinct from the epitope bound by 7C12, 2H11 or 8E11. The specification teaches that the C3b(I) antibody is useful for enhancing ADCC of tumor cells in vivo, as C3b(I) is tumor marker for a broad genus of malignancies. The specification does not teach any qualitative or quantitative difference in ADCC that could be attributed to the particular anti-C3b(I) antibody administered, such as isotype of epitope of C3b(I) bound by the antibody, nor does the specification teach a synergistic or additive effect of administering more than one anti-C3b(I)

antibody. Further, the specification does not teach or suggest that C3b(I), when deposited on IgM or IgG would be physically altered as to exhibit a different binding specificity with respect to a particular anti-C3b(I) antibody. There are no teaching in the specification or any art of record giving guidance as to the proximity of tumor antigens and the location of C3b(I) deposition on the cell surface, therefore, one of skill in the art would not know how to make or screen for antibodies which preferentially bound C3b(I) associated with IgM, IgG, tumor cell proteins or lipids. Given the lack of guidance in the specification, one of skill in the art would be subject to undue experimentation in order to practice the broadly claimed method, as it appears that all the antibodies taught by the specification would elicit the same result in terms of ADCC.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 23, 35- 37, 40-42, 44, 45 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irie (Proceedings of the AACR, 1975, Vol. 16, p. 170) and Michael et al (FASEB, 1993, Vol. 7, p. A375 and Howard and Hughes-Jones (Complement-Mediated Lysis

with Monoclonal Antibodies, In: Monoclonal Antibody Therapy, 1988, Vol. 45, pp. 3) and Neri et al (European Journal of Gynaecological Oncology, 1983, Vol. 4, pp. 37-40) in view of Perlmann et al (Journal of Experimental Medicine, 1981, Vol. 153, pp. 1592-1603). Claim 23 is drawn to a method of treating or preventing cancer in an animal, said method comprising , administering to the animal an anti-C3b(I) antibody. Claims 35, 36 and 37 embody the administration of IgG, IgM and complement components, respectively. Claims 40-42 embody the administration of combinations of IgM and complement and IgG and complement. Claim 44 further embodies the administration of plasma. Claims 45 and 46 embody the animal as a mammal and as a human, respectively. Irie teaches that human cancer cells react with humoral antibodies such as IgG, IgM and IgA to fix C3, but that non-cancerous cells do not fix C3. Michael et al teach that malignant epithelium synthesizes iC3b. Neri et al teach an immunoassay for circulating c3bi and correlates the level of C3bi in blood with the presence of a malignancy. Howard and Hughes-Jones teach C3b(I) as the most important opsonin present on a target surface, and that the extent of phagocytosis of a target cell coated with C3b(I) is greatly enhanced by IgG also attached to the surface of said cell. Thus Irie and Michael et al and Howard and Hughes-Jones and Neri et al teach C3bi as a tumor antigen. Neither Irie nor Michael et al nor Neri et al teach a method of treating or preventing cancer by the administration of a anti-C3b(I) antibody. Perlmann et al teaches that target cells having C3bi were lysed by lymphocytes only in the presence of antibody, and C3bi enhanced ADCC more strongly than other complement fragments such as C3b or C3d. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to treat cancer by administering an anti-C3bi antibody immunospecific for iC3bi to stimulate antibody dependent cytotoxicity in addition to administering IgG, IgM and complement components. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Irie on the complement fixation of cancer cells associated with the presence of IgM and IgG, and the teachings of Michael et al and Neri et al on C3b(I) as a tumor marker and the teachings of Perlmann et al on the enhancement of ADCC by iC3b.

7. Claim 25, 29, 30 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irie (Proceedings of the AACR, 1975, Vol. 16, p. 170) and Michael et al (FASEB, 1993, Vol. 7, p. A375 and Howard and Hughes-Jones (Complement-Mediated Lysis with Monoclonal Antibodies, In: Monoclonal Antibody Therapy, 1988, Vol. 45, pp. 3) and Neri et al (European Journal of Gynaecological Oncology, 1983, Vol. 4, pp. 37-40) and Perlmann et al (Journal of Experimental Medicine, 1981, Vol. 153, pp. 1592-1603) as applied to claims 23, 35- 37, 40-42, 44, 45 and 46 above, and further in view of Deo et al (Journal of Immunology, 1998 Feb 15, Vol. 160, pp. 1677-1686). Claim 25 is drawn to the method of claim 23 further incorporating the use of an antibody immunospecific for a cancer cell antigen. Claim 29 embodies the use of the anti-C3b(I) antibody as a bispecific antibody which is immunospecific for C3b(I) and an effector cell receptor or antigen. Claim 30 embodies various immune effector cells. Claim 32 embodies various effector cell marker antigens. For the reasons stated in paragraph 6, supra, the combination of Irie and Michael et al and Howard and Hughes-Jones and Neri et al and Perlmann et al render obvious a method of treating or preventing cancer by the administration of an anti-C3b(I) antibody. However, these prior art references do not teach a method of treatment comprising the use of an additional antibody immunospecific for a tumor antigen, or a bi-specific antibody which binds C3b(I) in addition to an effector cell antigen. Deo teaches the use of bispecific antibodies directed toward both tumor antigens and effector cell antigens to promote ADCC. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use an additional antibody that binds to a tumor cell antigen, or use a bispecific antibody that binds to C3b(I) and an effector cell antigen. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Deo et al on the efficacy of bispecific antibodies linking tumor cells to effector cell antigens for enhancing cell-mediated cytotoxicity of tumor targets.

8. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Irie (Proceedings of the AACR, 1975, Vol. 16, p. 170) and Michael et al (FASEB, 1993, Vol. 7, p. A375 and Howard and Hughes-Jones (Complement-Mediated Lysis with Monoclonal Antibodies, In:

Monoclonal Antibody Therapy, 1988, Vol. 45, pp. 3) and Neri et al (European Journal of Gynaecological Oncology, 1983, Vol. 4, pp. 37-40) and Perlmann et al (Journal of Experimental Medicine, 1981, Vol. 153, pp. 1592-1603) and Deo et al (Journal of Immunology, 1998 Feb 15, Vol. 160, pp. 1677-1686) as applied to claims 25, 29, 30 and 32 above, and further in view of Paul (Immunology, pg 934). Claim 31 specifically embodies a bi-specific antibody directed toward C3b(I) and an erythrocyte antigen. For the reasons set forth in paragraph 7, supra, the prior art references render obvious the use of a bi-specific antibody directed towards C3b(I) and a phagocytic cell. The prior art references do not teach a bi-specific antibody directed toward an erythrocyte. Paul teaches that the CR1 receptors of erythrocytes functions in clearing immune complexes from the circulation, and further allowing phagocytosis of said immune complexes by macrophage. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use a bi-specific antibody directed toward C3b(I) and the CR1 antigen of erythrocytes. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Paul on the importance of erythrocytes in the handling the clearance of immune complexes that arise during the humoral immune response.

9. Claims 33, 34, 39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irie (Proceedings of the AACR, 1975, Vol. 16, p. 170) and Michael et al (FASEB, 1993, Vol. 7, p. A375 and Howard and Hughes-Jones (Complement-Mediated Lysis with Monoclonal Antibodies, In: Monoclonal Antibody Therapy, 1988, Vol. 45, pp. 3) and Neri et al (European Journal of Gynaecological Oncology, 1983, Vol. 4, pp. 37-40) and Perlmann et al (Journal of Experimental Medicine, 1981, Vol. 153, pp. 1592-1603) as applied to claims 23, 35- 37, 40-42, 44, 45 and 46 above, and further in view of Schlom (Monoclonal Antibodies, In: Molecular Foundations of Oncology, 1991, pp. 95-134). Claims 33 and 34 embody an anti-C3b(I) monoclonal antibody and a humanized antibody, respectively. Claims 39 and 43 embody the conjugation of the anti-C3b(I) antibody to a therapeutic agent and a detectable agent, respectively. For the reasons stated in paragraph 6, supra, the combination of Irie and Michael et

al and Howard and Hughes-Jones and Neri et al and Perlmann et al render obvious a method of treating or preventing cancer by the administration of an anti-C3b(I) antibody. However the prior art references do not teach the use of a monoclonal or humanized anti-C3b(I) antibody or an anti-C3b(I) antibody conjugated to a therapeutic or detectable reagent. Schlom teaches monoclonal antibodies, humanized antibodies, and monoclonal antibodies conjugated to therapeutic or detectable labels. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use a monoclonal antibody to C3b(I), a humanized C3b(I) antibody or any of the affor said conjugated with a detectable or therapeutic reagent. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Schlom on the advantages of using monoclonal or humanized antibodies in human therapy, and the success of using monoclonal antibodies conjugated to detectable or therapeutic labels for imaging or treating tumors.

10. Claims 24, 26 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Irie (Proceedings of the AACR, 1975, Vol. 16, p. 170) and Michael et al (FASEB, 1993, Vol. 7, p. A375 and Howard and Hughes-Jones (Complement-Mediated Lysis with Monoclonal Antibodies, In: Monoclonal Antibody Therapy, 1988, Vol. 45, pp. 3) and Neri et al (European Journal of Gynaecological Oncology, 1983, Vol. 4, pp. 37-40) and Perlmann et al (Journal of Experimental Medicine, 1981, Vol. 153, pp. 1592-1603) and Deo et al (Journal of Immunology, 1998 Feb 15, Vol. 160, pp. 1677-1686) in view of Carson et al (US 5,985,847). Claims 24 and 26 are drawn to the methods of claims 23 and 25 respectively, with the substitution of nucleic acids encoding the anti-C3b(I) in place of the anti-C3b(I) antibody polypeptide. For the reasons stated in paragraph 7, supra, the prior art references render obvious the administration of the anti-C3b(I) polypeptide. However, the prior art references do not teach the administration of nucleic acids encoding the anti-C3b(I) antibody or complement peptides. Carson et al teaches methods for the administration of nucleic acids encoding biologically active peptide and antibodies. It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed

invention was made to administer the nucleic acids encoding the anti-C3b(I) antibody or complement in place of the anti-C3b(I) antibody polypeptide or complement polypeptides. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Carson et al on the efficacy of administering nucleic acids encoding biologically active peptides.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Patent Examiner, Group 1642
November 2, 2001